

1976 - 1977
ANNUAL REPORT

RESOURCE-RELATED RESEARCH
COMPUTERS AND CHEMISTRY

Grant No. RR-00612

BIOTECHNOLOGY RESOURCES PROGRAM
OF THE
NATIONAL INSTITUTES OF HEALTH

February, 1977

COMPUTER SCIENCE DEPARTMENT
STANFORD UNIVERSITY

SECTION I

DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICEAPPLICATION
FOR CONTINUATION GRANT

| | | | |
|-------------------------|-----------|------------------|--|
| REVIEW GROUP SSS | TYPE 5 | PROGRAM R24 | GRANT NUMBER (Insert on all pages) RR-00612 |
| TOTAL PROJECT PERIOD | | | |
| From: 5/1/74 | | Through: 4/30/77 | |
| REQUESTED BUDGET PERIOD | | | |
| From: 8/1/76 | | Through: 4/30/77 | |

1. TITLE

Resource-Related Research Computers and Chemistry

2A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR
(Name and Address, Street, City, State, Zip Code)DJERASSI, CARL
STANFORD UNIVERSITY
DEPT. OF CHEMISTRY
STANFORD, CALIF. 94305

4. APPLICANT ORGANIZATION (Name and Address-Street, City, State, Zip Code)

STANFORD UNIVERSITY

2B. DEGREE

PH.D.

2C. SOCIAL SECURITY NO.

5. PHS ACCOUNT NUMBER

1941156365A1

2D. DEPARTMENT, SERVICE, LABORATORY OR EQUIPMENT

CHEMISTRY

6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE OF APPLICANT ORGANIZATION

DEPUTY V. P. FOR BUSINESS & FINANCE
STANFORD UNIVERSITY
STANFORD, CALIF. 94305

2E. MAJOR SUBDIVISION

SCH. OF HUMANITIES AND SCIENCES

3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR INSTITUTIONAL GRANT PURPOSES

20 OTHER

7. RESEARCH INVOLVING HUMAN SUBJECTS (See Instructions)

☒ No ☐ Yes APPROVED

Date

8. INVENTIONS (See Instructions)

☒ No☐ Yes-not previously reported☐ Yes previously reported

9. PERFORMANCE SITE(S)

STANFORD UNIVERSITY
DEPARTMENT OF CHEMISTRY
COMPUTER SCIENCE DEPARTMENT
DEPARTMENT OF GENETICS
STANFORD, CALIF. 94305

TELEPHONE INFORMATION

11A. PRINCIPAL INVESTIGATOR

Area
Code

Tele. No. & Ext.

OR
PROGRAM DIRECTOR (Item 2a)

415

497-2783

11B. Name of business official (Item 6)

K. D. Creighton

415

497-2251

11C. Name and title of administrative official (Item 15b)

D'Ann B. Downey,
Sponsored Projects Dir.

415

497-2883

10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD

\$129,931.00

12A. CONGRESSIONAL DISTRICT OF APPLICANT ORGANIZATION SHOWN IN ITEM 4

TWELFTH

12B. COUNTY OF APPLICANT ORGANIZATION SHOWN IN ITEM 4

SANTA CLARA

13. DO NOT USE THIS SPACE

14. CERTIFICATION AND ACCEPTANCE. We, the undersigned, certify that the statements herein are true and complete to the best of our knowledge and accept, as to any grant awarded, the obligation to comply with Public Health Service terms and conditions in effect at the time of the award.

15. SIGNATURES

(Signatures required on original copy only. Use ink. "Per" signatures not acceptable.)

15A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

DATE

15B. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION

DATE

SECTION II

SECTION II—BUDGET (USUALLY 12 MONTHS)

FROM
May, 1977THROUGH
April, 1978GRANT NUMBER
RR-00612

A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD

| PERSONNEL NAME (Last, First, Initial) (a) | TITLE OF POSITION (b) | TIME OR EFFORT %/HRS. (c) | SALARY REQUESTED (d) | FRINGE BENEFITS (See Instructions) (e) | TOTAL (f) |
|--|--------------------------|------------------------------------|----------------------------|--|--------------|
| | PRINCIPAL INVESTIGATOR | | | | |
| See Proposal for Continued Research 1977-80 Submitted May, 1976 | | | | | |
| Subtotals → | | | \$ | \$ | |
| (Indicate cost of each item listed below) | | | | | |
| TOTAL (Columns (d) and (e)) → | | | | | \$ |
| CONSULTANT COSTS (See Instructions) | | | | | \$ |
| EQUIPMENT | | | | | \$ |
| SUPPLIES | | | | | \$ |
| TRAVEL | | | | | \$ |
| DOMESTIC | | | | | \$ |
| FOREIGN | | | | | \$ |
| PATIENT COSTS (See instructions) | | | | | \$ |
| ALTERATIONS AND RENOVATIONS | | | | | \$ |
| OTHER EXPENSES (Itemize) | | | | | \$ |
| TOTAL DIRECT COST (Enter on Page 1, Item 10) | | | | | \$ |

INDIRECT
COST

(See Instructions)

% S&W*

% TDC*

*If this is a special rate (e.g. off-site), explain.

Date of DHEW Agreement:

☐ Not Requested☐ Under negotiation with

SECTION II—BUDGET (Continued)

Grant Number

RR-00612

B. Supplemental information regarding ITEMS in the proposed budget for the next period which require explanation or justification. (See instructions)

See Proposal for Continued Research

1977-80

submitted May, 1976

SECTION III

**SECTION III—FISCAL DATA FOR
CURRENT BUDGET PERIOD**

(USUALLY 12 MONTHS)

FROM

8/1/76

THROUGH

4/30/77

GRANT NUMBER

RR-00612

The following pertains to your CURRENT PHS budget. Do not include cost sharing funds. This information in conjunction with that provided on Page 2 will be used in determining the amount of support for the NEXT budget period.

| A. BUDGET CATEGORIES | | CURRENT BUDGET (As approved by awarding unit) (1) | ACTUAL EXPENDITURES THRU 1/31/77 (Insert Date) (2) | ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD (3) | TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3) (4) | ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1) (5) |
|---------------------------------------|----------|---|---|---|--|--|
| Personnel (Salaries) | | 100,761 | 59,784 | 36,593 | 96,377 | 4,384 |
| Fringe Benefits | | 18,943 | 11,144 | 6,953 | 18,097 | 846 |
| Consultant Costs | | - | - | - | - | - |
| Equipment | | - | - | - | - | - |
| Supplies | | - | 50 | 10 | 60 | (60) |
| TRAVEL | Domestic | 1,400 | 1,509 | 1,741 | 3,250 | (1,850) |
| | Foreign | | | | | |
| Patient Costs | | | | | | |
| Alterations and Renovations | | | | | | |
| *Other | | 8,827 | 7,355 | 4,585 | 11,940 | (3,113) |
| Total Direct Costs | | 129,931 | 79,842 | 49,882 | 129,724 | 207 |
| Indirect Costs (If included in award) | | | | | | |
| TOTALS → | | \$ 129,931 | \$ 79,842 | \$ 49,882 | \$ 129,724 | \$ 207 |

Use space below to:

B. List all items of equipment purchased or expected to be purchased during this budget period which have a unit cost of \$1000 or more.

C. Explain any significant balance or deficit shown in any category of Column 5.

D. List all other research support for Principal Investigator by source, project title, and annual amount.

B. Equipment Purchased

| | | | | | |
|--|-------|-------|-------|--------|---------|
| Terminal Rental | 3,587 | 3,957 | 1,800 | | |
| Telephone | 2,100 | 2,340 | 1,080 | | |
| Publications and Technical services | 2,900 | 984 | 1,600 | | |
| Postage | 240 | 74 | 105 | 11,940 | (3,113) |

D. Research Support for Principal Investigator

| | | |
|-------------|---|-----------|
| NIH AM04257 | Mass Spectrometry in Organic Biochemistry | \$ 67,700 |
| NIH GM06840 | Marine chemistry with special Emphasis on Steroids | 101,490 |
| NIH GM20276 | Applications of Magnetic Circular Dichroism | 40,834 |

SECTION IV

| | | | |
|---|--|-------------------------------|---------|
| APPLICANT: REPEAT GRANT NUMBER SHOWN ON PAGE 1 → | | GRANT NUMBER | |
| SECTION IV—SUMMARY PROGRESS REPORT | | RR-00612 | |
| PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Last, First, Initial) | | PERIOD COVERED BY THIS REPORT | |
| NAME OF ORGANIZATION | | FROM | THROUGH |
| | | 8/1/76 | 4/30/77 |
| TITLE (Repeat title shown in Item 1 on first page) | | | |

1. List publications: (a) published and not previously reported; (b) in press. Provide five reprints if not previously submitted.
2. List all additions and deletions in professional personnel and any changes in effort.
3. Progress Report. (See Instructions)

Progress Report Follows

Resource Related Research - Computers & Chemistry

Stanford University
NIH/BRP Grant RR-00612

Carl Djerassi, Principal Investigator
(Social Security No.)

Research Highlights (1976-77)

1. One of the DENDRAL programs, named CONGEN, continued to be used by working scientists on problems of biomedical importance. CONGEN is a complex symbol-manipulation program that helps working scientists develop hypotheses about the molecular structure of organic chemical compounds. The scientist provides structural inferences, the program provides the result of combining the scientist's partial hypotheses in all plausible ways. Several scientists across the nation have used the CONGEN program to help them elucidate molecular structures of naturally-occurring compounds. We anticipate continued use of this program, and similar ones, as scientists realize how helpful they can be for structure elucidation.

2. The Meta-DENDRAL program successfully formulated rules of mass spectrometry that were new to the science. These rules, along with a discussion of the methodology, were published in the scientific literature [Jnl Am Chem Soc, 98:6168 (1976)]. The

program was tested to see if it could rediscover the rules of mass spectrometry for two classes of chemical compounds that were already well understood (amines and estrogenic steroids). Then it was applied to three classes of compounds whose behavior in a mass spectrometer was not as well known (mono-, di-, and tri-ketoandrostanes). The program produced three sets of rules that explained much of the significant data for these classes. The time for manual rule formation for these data was estimated to be several months.

Table of Contents

| Section | Page |
|--|------|
| Subsection | |
| 1. OVERVIEW OF RESEARCH ACTIVITIES | 1 |
| 2. EXPERIMENT PLANNER | 5 |
| 3. Applications of REACT to Structure Elucidation Problems | 9 |
| 4. CONGEN Developments | 15 |
| 4.1 Intelligent use of constraining substructural information | 15 |
| 4.2 New tools for post-pruning CONGEN structures. | 19 |
| 5. USE OF CONGEN BY OTHER SCIENTISTS | 24 |
| 5.1 Chemists Using Exported Programs | 24 |
| 5.2 Remote Users of SUMEX | 26 |
| 5.3 Chemists Communicating by Mail | 26 |
| 5.4 Chemical Problems Posed to CONGEN | 26 |
| 6. Stereochemistry in CONGEN | 30 |
| 6.1 Algorithm | 30 |
| 6.2 Programming Progress | 31 |
| 7. The GC/HRMS DATA SYSTEM | 32 |
| 7.1 Improvements to the Data System | 32 |

| | | |
|-----|---|----|
| 7.2 | Changes in the Operating System | 34 |
| 7.3 | New Developments | 35 |
| 8. | META DENDRAL | 36 |
| 9. | C13 NMR SPECTROMETRY | 38 |
| 10. | BUDGET | 40 |
| 11. | RECENT PUBLICATIONS OF THE HEURISTIC PROGRAMMING PROJECT | 41 |